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## T-cadherin is critical for adiponectin-mediated cardioprotection in mice.

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### Public Summary:

The circulating, adipocyte-secreted hormone adiponectin (APN) exerts protective effects on the heart under stress conditions. The receptors binding APN to cardiac tissue, however, have remained elusive. Here, we report that the glycosyl phosphatidylinositol-anchored cell surface glycoprotein T-cadherin (encoded by *Cdh13*) protects against cardiac stress through its association with APN in mice. We observed extensive colocalization of T-cadherin and APN on cardiomyocytes in vivo. In T-cadherin-deficient mice, APN failed to associate with cardiac tissue, and its levels dramatically increased in the circulation. Pressure overload stress resulted in exacerbated cardiac hypertrophy in T-cadherin-null mice and paralleled corresponding defects in mice lacking APN. During ischemia-reperfusion injury, the absence of T-cadherin increased infarct size similar to that in APN-null mice. Myocardial AMPK is a major downstream protective signaling target of APN. In both cardiac hypertrophy and ischemia-reperfusion models, T-cadherin was necessary for APN-dependent AMPK phosphorylation. In APN-null mice, recombinant adenovirus-expressed APN reduced exaggerated hypertrophy and infarct size and restored AMPK phosphorylation as previously reported. In contrast, rescue was ineffective in mice lacking T-cadherin in addition to APN. These data suggest that T-cadherin protects from stress-induced pathological cardiac remodeling by binding APN and activating its cardioprotective functions.

### Scientific Abstract:

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